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TAK1 mediates lipopolysaccharide-induced RANTES promoter activation in BV-2 microglial cells. Mol Cells. 2002 Aug 31;14(1):35-42. PMID: 12243350 [PubMed - indexed for MEDLINE]

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TAK1 is a ubiquitin-dependent kinase of MKK and IKK. Nature. 2001 Jul 19;412(6844):346-51. PMID: 11460167 [PubMed - indexed for MEDLINE]

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The MAPK kinase kinase TAK1 plays a central role in coupling the interleukin-1 receptor to both transcriptional and RNA-targeted mechanisms of gene regulation. J Biol Chem. 2001 Feb 2;276(5):3508-16. Epub 2000 Oct 24. PMID: 11050078 [PubMed - indexed for MEDLINE]

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L5 ANSWER 1 OF 12 MEDLINE on STN DUPLICATE 1
AN 2005104514 IN-PROCESS
DN PubMed ID: 15725700
TI Nuclear receptors as targets for drug development: crosstalk
between
peroxisome proliferator-activated receptor gamma and **cytokines**
in bone marrow-derived mesenchymal stem cells.
AU Takada Ichiro; Suzawa Miyuki; Kato Shigeaki
CS Institute of Molecular and Cellular Bioscience, University of
Tokyo,
Japan.. itakada@iam.u-tokyo.ac.jp
SO Journal of pharmacological sciences, (2005 Feb) 97 (2) 184-9.
Electronic
Publication: 2005-02-11.
Journal code: 101167001. ISSN: 1347-8613.
CY Japan
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS NONMEDLINE; IN-PROCESS; NONINDEXED; Priority Journals
ED Entered STN: 20050301
Last Updated on STN: 20050316
AB Peroxisome proliferator-activated receptor gamma (PPARGamma) is a
ligand-dependent nuclear receptor and regulates adipogenesis and
fat
metabolism. PPARGamma is activated by fatty acid derivatives
and some
synthetic compounds such as the thiazolidinediones. In
addition, certain

cytokines were known to affect the transactivation function of PPARgamma. However, the molecular mechanism of the functional interaction between PPARgamma and **cytokine** signaling remains unclear. We found that combined treatment of PPARgamma and **cytokines** (IL-1 or TNF-alpha) inhibited adipogenesis and induced osteoblastogenesis in bone marrow-derived mesenchymal stem cells. Furthermore, we showed that the ligand dependent transactivation function of PPARgamma was suppressed by IL-1 and TNF-alpha. This suppression was mediated through NF-kappaB activated by the **TAK1/TAB1**-NIK cascade, a downstream cascade triggered with IL-1 or TNF-alpha signaling. Thus, we have identified a molecular mechanism of functional cross-talk between PPARgamma and **cytokine** signaling that may provide a theoretical basis for development of novel therapeutical strategies and design of novel compounds for treatment of obesity, diabetes, and some other chronic diseases.

L5 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2003:360779 CAPLUS

DN 138:380400

TI **TAK1-TAB1** fusion protein: a novel constitutively active mitogen-activated protein kinase kinase kinase for use in drug screening

IN Sugita, Naohisa; Sakurai, Hiroaki; Sato, Naoya

PA Tanabe Seiyaku Co., Ltd., Japan

SO Jpn. Kokai Tokkyo Koho, 34 pp.

CODEN: JKXXAF

DT Patent

LA Japanese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.
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DATE

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PI	JP 2003135070	A2	20030513	JP 2001-335988
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20011101

PRAI	JP 2001-335988	20011101
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AB A fusion protein comprising human transforming growth factor- β -activated kinase 1 (TAK1) N-terminal MAPKKK domain and human **TAK1** binding protein 1 (**TAB1**) C-terminal **TAK1** activation domain, functional as active mutant TAK1, encoding cDNAs, recombinant

expression, and use in screening TAK1 inhibitors, are disclosed. **TAK1** and **TAB1** are connect via a linker peptide.

Activation of JNK, p38, or IKK, or induction of **cytokine** production, such as IL-6, IL-1, or TNF, may be assayed for

screening. TAK1 mitogen-activated protein kinase kinase kinase (MAP3K) is

activated by its specific activator, **TAK1-binding protein 1 (TAB1)**. A constitutively active TAK1 mutant has not yet been generated due to the indispensable requirement of **TAB1** for **TAK1** kinase activity. In this study, the authors generated a novel constitutively active TAK1 by fusing its kinase domain to

the

minimal **TAK1**-activation domain of **TAB1**.

Co-immunopptn. assay demonstrated that these domains interacted intra-molecularly. The **TAK1-TAB1** fusion protein

showed a significant MAP3K activity in vitro and activated c-Jun N-terminal kinase/p38 MAPKs and I κ B kinase in vivo, which was followed by increased production of interleukin-6. These

results indicate

that the fusion protein is useful for characterizing the physiol. roles of the **TAK1-TAB1** complex.

L5 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2003:883731 CAPLUS

DN 139:394860

TI Feedback control of the protein kinase TAK1 by SAPK2a/p38 α

AU Cheung, Peter C. F.; Campbell, David G.; Nebreda, Angel R.; Cohen, Philip

CS MSI/WTB Complex, School of Life Sciences, MRC Protein Phosphorylation

Unit, University of Dundee, Dundee, DD1 5EH, UK

SO EMBO Journal (2003), 22(21), 5793-5805

CODEN: EMJODG; ISSN: 0261-4189

PB Oxford University Press

DT Journal

LA English

AB TAB1, a subunit of the kinase TAK1, was phosphorylated by SAPK2a/p38 α at Ser423, Thr431 and Ser438 in vitro. TAB1 became phosphorylated at all three sites when cells were exposed to cellular

stresses, or stimulated with tumor necrosis factor- α (TNF- α), interleukin-1 (**IL-1**) or **lipopolysaccharide** (

LPS). The phosphorylation of Ser423 and Thr431 was prevented if cells were pre-incubated with SB 203580, while the

phosphorylation of

Ser438 was partially inhibited by PD 184352. Ser423 is the first residue

phosphorylated by SAPK2a/p38 α that is not followed by proline.

The

activation of TAK1 was enhanced by SB 203580 in **LPS**-stimulated macrophages, and by proinflammatory **cytokines** or osmotic shock in epithelial KB cells or embryonic fibroblasts. The activation

of TAK1

by TNF- α , **IL-1** or osmotic shock was also

enhanced in embryonic fibroblasts from SAPK2a/p38 α -deficient mice,

while incubation of these cells with SB 203580 had no effect.
Our results suggest that TAB1 participates in a SAPK2a/p38 α -mediated feedback control of TAK1, which not only limits the activation of SAPK2a/p38 α but synchronizes its activity with other signalling pathways that lie downstream of TAK1 (JNK and IKK).

RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2003:118999 CAPLUS

DN 139:33778

TI TAB2 is essential for prevention of apoptosis in fetal liver but not for

interleukin-1 signaling

AU Sanjo, Hideki; Takeda, Kiyoshi; Tsujimura, Tohru;

Ninomiya-Tsuji, Jun;

Matsumoto, Kunihiro; Akira, Shizuo

CS Department of Host Defense, Research Institute for Microbial Diseases,

Osaka University, Osaka, 565-0871, Japan

SO Molecular and Cellular Biology (2003), 23(4), 1231-1238

CODEN: MCEBD4; ISSN: 0270-7306

PB American Society for Microbiology

DT Journal

LA English

AB The proinflammatory **cytokine** interleukin-1 (IL-1) transmits a signal via several critical cytoplasmic proteins such

as MyD88, IRAKs and TRAF6. Recently, serine/threonine kinase TAK1 and

TAK1 binding protein 1 and 2 (TAB1/2) have been identified as mols.

involved in IL-1-induced TRAF6-mediated activation of AP-1 and NF- κ B via mitogen-activated protein (MAP) kinases and I κ B kinases, resp. However, their physiol. functions remain to be

clarified. To elucidate their roles in vivo, we generated TAB2-deficient

mice. The TAB2 deficiency was embryonic lethal due to liver degeneration

and apoptosis. This phenotype was similar to that of NF- κ B p65-,

IKK β -, and NEMO/IKK γ -deficient mice. However, the IL-1-induced activation of NF- κ B and MAP kinases was not impaired in TAB2-deficient embryonic fibroblasts. These findings demonstrate that TAB2 is essential for embryonic development through

prevention of liver apoptosis but not for the IL-1

receptor-mediated signaling pathway.

RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 5 OF 12 MEDLINE on STN DUPLICATE 2
AN 2003132605 MEDLINE
DN PubMed ID: 12598905
TI **Cytokines** suppress adipogenesis and PPAR-gamma function through
the **TAK1/TAB1**/NIK cascade.
AU Suzawa Miyuki; Takada Ichiro; Yanagisawa Junn; Ohtake Fumiaki;
Ogawa
 Satoko; Yamauchi Toshimasa; Kadowaki Takashi; Takeuchi Yasuhiro;
Shibuya
 Hiroshi; Gotoh Yukiko; Matsumoto Kunihiro; Kato Shigeaki
CS Institute of Molecular and Cellular Biosciences, University of
Tokyo,
 Yayoi, Bunkyo-ku, Tokyo 113-0032, Japan.
SO Nature cell biology; (2003 Mar) 5 (3) 224-30.
 Journal code: 100890575. ISSN: 1465-7392.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200304
ED Entered STN: 20030321
 Last Updated on STN: 20030422
 Entered Medline: 20030421
AB Pluripotent mesenchymal stem cells in bone marrow differentiate
into
 adipocytes, osteoblasts and other cells. Balanced
cytodifferentiation of
 stem cells is essential for the formation and maintenance of
bone marrow;
 however, the mechanisms that control this balance remain largely
unknown.
 Whereas **cytokines** such as interleukin-1 (**IL-1**
) and tumour-necrosis factor-alpha (TNF-alpha) inhibit
adipogenesis, the
 ligand-induced transcription factor peroxisome
proliferator-activated
 receptor-gamma (PPAR-gamma), is a key inducer of adipogenesis.
Therefore,
 regulatory coupling between **cytokine**- and PPAR-gamma-mediated
signals might occur during adipogenesis. Here we show that the
ligand-induced transactivation function of PPAR-gamma is
suppressed by
 IL-1 and TNF-alpha, and that this suppression is
mediated through NF-kappaB activated by the **TAK1/TAB1**
 /NF-kappaB-inducing kinase (NIK) cascade, a downstream cascade
associated
 with **IL-1** and TNF-alpha signalling. Unlike
suppression of the PPAR-gamma transactivation function by

mitogen-activated protein kinase-induced growth factor
signalling through
phosphorylation of the A/B domain, NF-kappaB blocks PPAR-gamma
binding to
DNA by forming a complex with PPAR-gamma and its AF-1-specific
co-activator PGC-2. Our results suggest that expression of IL-
1 and TNF-alpha in bone marrow may alter the fate of pluripotent
mesenchymal stem cells, directing cellular differentiation
towards
osteoblasts rather than adipocytes by suppressing PPAR-gamma
function
through NF-kappaB activated by the **TAK1/TAB1/NIK**
cascade.

L5 ANSWER 6 OF 12 BIOSIS COPYRIGHT (c) 2005 The Thomson
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AN 2003:568462 BIOSIS

DN PREV200300563327

TI SALMONELLA FLAGELLIN ACTIVATES A NOVEL GP91-PHOX ISOFORM (NOX1)
EXPRESSED

IN COLONIC EPITHELIAL CELLS.

AU Rokutan, Kazuhito [Reprint Author]; Kuwano, Yuki; Kawahara,
Tsukasa;

Kodama, Nanae; Kondo-Teshima, Shigetada; Nakamura, Keiya

CS Tokushima, Tokushima, Japan

SO Digestive Disease Week Abstracts and Itinerary Planner, (2003)
Vol. 2003,

pp. Abstract No. T1092. e-file.

Meeting Info.: Digestive Disease 2003. FL, Orlando, USA. May
17-22, 2003.

American Association for the Study of Liver Diseases; American
Gastroenterological Association; American Society for
Gastrointestinal

Endoscopy; Society for Surgery of the Alimentary Tract.

DT Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 3 Dec 2003

Last Updated on STN: 3 Dec 2003

AB BACKGROUNDS/AIMS: Reactive oxygen species (ROS) regulate a
variety of

biological processes. During the last two years, the cDNAs for
six new

homologs of human gp91-phox have been cloned: NADPH oxidase
(Nox)/dual

oxidase (Duox) family. Among the Nox/Duox family, Nox1 is
predominantly

expressed in the human colon, while its pathophysiological roles
are not

fully understood. We report here that the colonic Nox1 is
sensitive to

Salmonella flagellin and increases superoxide generation
possibly through

the TLR5 signaling. MATERIAL AND METHODS: Primary cultures of guinea pig large intestinal epithelial cells and human cancer cell lines (Caco2, T84, and HT29 cells) were used in this study. Expression of the Nox/Duox isozyme transcripts were examined by RT-PCR, and all of the isozyme proteins and the cytosolic components of phagocyte NADPH oxidase (p22-phox, p67-phox, p47-phox, p40-phox, and rac1/2) were measured by immunoblot analysis with specific antibodies against the respective proteins. Transduction of p67-phox, p47-phox, and dominant negative MyD88 was performed using respective adenovirus vectors. RESULTS: The primary cultures secreted large amounts of superoxide (150 nmol/mg protein/h), while the cell lines produced small amounts (2-3 nmol/mg protein/h). Among the Nox/Duox family, only Nox1 isoform was expressed in the colonic epithelial cells tested. Primary cultured cells also expressed p22-phox, p67-phox, and rac1, but cancer cell lines possessed p22-phox and rac1. Overexpression of p67-phox failed to increase superoxide generation in Caco2 cells, but co-transfection of p67-phox and p47-phox up-regulated the production 10-fold. None of cytokines (IL-1-beta, TNF-alpha, and IFN-gamma), growth factors (EGF and TGF-beta), E. coli LPS, and PMA up-regulated the Nox1 activity. Salmonella flagellin (FliC) stimulated constitutively expressed TLR5 in Caco2 cells, phosphorylated TAK1/TAB1, and increased superoxide production 2-fold. This up-regulation was cancelled by dominant negative MyD88. DISCUSSION: Our results show that the cytosolic components (p67-phox and/or p47-phox) are required for full activation of the potent Nox1 expressed in colonic epithelial cells. Nox1 expressed on surface mucous cells of the colon may play an important role in host epithelial cell-bacterial interactions for host defense.

AN 2004:193972 BIOSIS
 DN PREV200400194532
 TI TAK1 - mediated induction of nitric oxide synthase and **cytokine** gene expression in glial cells.
 AU White, S. [Reprint Author]; Shen, Q. [Reprint Author]; Fan, F. [Reprint Author]; Griesemer, D. [Reprint Author]; Bhat, N. R. [Reprint Author]
 CS Neurol., Med. Univ. of South Carolina, Charleston, SC, USA
 SO Society for Neuroscience Abstract Viewer and Itinerary Planner, (2003)
 Vol. 2003, pp. Abstract No. 103.12. <http://sfn.scholarone.com>. e-file.
 Meeting Info.: 33rd Annual Meeting of the Society of Neuroscience. New Orleans, LA, USA. November 08-12, 2003. Society of Neuroscience.
 DT Conference; (Meeting)
 Conference; Abstract; (Meeting Abstract)
 LA English
 ED Entered STN: 14 Apr 2004
 Last Updated on STN: 14 Apr 2004
 AB Inflammatory cell signaling leading to transcriptional activation is primarily mediated by signal transduction via mitogen-activated protein kinase (MAPK) and NFKAPPAB pathways. A common upstream kinase that signals the activation of these pathways is TGFbeta-activated kinase1 (TAK1), which itself becomes activated in response to **cytokines** and upon engagement of a class of cell surface receptors involved in innate immunity i.e., Toll-like receptors (TLRs) by bacterial and viral pathogens. This study directly tests the role of TAK1 in the induction of inducible nitric oxide (NO) synthase (iNOS) and **cytokines** in glial cells, the immune-regulatory cells of the CNS, by transient transfection assays. Transfection of C-6 glia and a rat microglial cell line with TAK1 (but not its inactive form) along with its activator protein i.e., **TAK1**-binding protein 1 (**TAB1**) resulted in a marked stimulation of a co-transfected rat iNOS promoter-reporter construct (iNOS-Luc). TAK1-induced iNOS-Luc activity was substantially inhibited by pharmacological inhibitors of the known down-stream kinases i.e., p38 MAPK and JNK (i.e., SB203580 and SP620125) and was almost completely blocked by co-expression of a phosphorylation mutant of

IKAPPAB. **TAK1/TAB1** also induced the production of NO and the expression of iNOS and the **cytokine** i.e., IL-1beta in microglial cells in a p38 MAPK-, JNK-and NFKAPPAB-dependent manner. The results of these studies provide evidence for an important role for TAK1-mediated intracellular signaling, via p38 MAPK, JNK and NFKAPPAB, in the transcriptional activation of iNOS and **cytokine** genes in glial cells.

L5 ANSWER 8 OF 12 MEDLINE on STN . DUPLICATE 3
AN 2001269992 MEDLINE
DN PubMed ID: 11050078
TI The MAPK kinase kinase TAK1 plays a central role in coupling the interleukin-1 receptor to both transcriptional and RNA-targeted mechanisms of gene regulation.
AU Holtmann H; Enninga J; Kalble S; Thiefes A; Dorrie A; Broemer M; Winzen R; Wilhelm A; Ninomiya-Tsuji J; Matsumoto K; Resch K; Kracht M
CS Institute of Pharmacology, Medical School Hannover, Carl-Neuberg-Strasse 1, D-30625 Hannover, Germany.
SO Journal of biological chemistry, (2001 Feb 2) 276 (5) 3508-16. Electronic
Publication: 2000-10-24.
Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200106
ED Entered STN: 20010625
Last Updated on STN: 20030105
Entered Medline: 20010621
AB Mechanisms of fulminant gene induction during an inflammatory response were investigated using expression of the chemoattractant cytokine interleukin-8 (IL-8) as a model. Recently we found that coordinate activation of NF-kappaB and c-Jun N-terminal protein kinase (JNK) is required for strong IL-8 transcription, whereas the p38 MAP kinase (MAPK) pathway stabilizes the IL-8 mRNA. It is unclear how these pathways are coupled to the receptor for IL-1, an important physiological inducer of IL-8. Expression of the MAP kinase kinase kinase (MAPKKK) **TAK1** together with its coactivator **TAB1** in

HeLa cells activated all three pathways and was sufficient to induce IL-8 formation, NF-kappaB + JNK2-mediated transcription from a minimal IL-8 promoter, and p38 MAPK-mediated stabilization of a reporter mRNA containing IL-8-derived regulatory mRNA sequences. Expression of a kinase-inactive mutant of TAK1 largely blocked IL-1-induced transcription and mRNA stabilization, as well as formation of endogenous IL-8. Truncated **TAB1**, lacking the **TAK1** binding domain, or a TAK1-derived peptide containing a TAK1 autoinhibitory domain were also efficient in inhibition. These data indicate that the previously described three-pathway model of IL-8 induction is operative in response to a physiological stimulus, IL-1, and that the MAPKKK TAK1 couples the IL-1 receptor to both transcriptional and RNA-targeted mechanisms mediated by the three pathways.

L5 ANSWER 9 OF 12 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

AN 2002:4979 BIOSIS

DN PREV200200004979

TI Inhibition of adipogenesis by **cytokines** with suppression of PPARgamma function through **TAK1/TAB1**-NIK promotes osteoblastogenesis.

AU Suzawa, M. [Reprint author]; Takada, I. [Reprint author]; Yanagisawa, J.

[Reprint author]; Takeuchi, Y.; Goroh, Y. [Reprint author]; Matsumoto, K.;

Kato, S. [Reprint author]

CS IMBC, University of Tokyo/CREST, Tokyo, Japan

SO Journal of Bone and Mineral Research, (September, 2001) Vol. 16, No.

Suppl. 1, pp. S496. print.

Meeting Info.: Twenty-Third Annual Meeting of the American Society for

Bone and Mineral Research. Phoenix, Arizona, USA. October 12-16, 2001.

CODEN: JBMREJ. ISSN: 0884-0431.

DT Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 28 Dec 2001

Last Updated on STN: 25 Feb 2002

L5 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2000:278128 CAPLUS

DN 132:320956

TI Method for screening compound inhibiting signal transduction of inflammatory **cytokine**

IN Tsuchiya, Masayuki; Ohtomo, Toshihiko; Sugamata, Yasuhiro; Matsumoto, Kunihiro

PA Chugai Seiyaku K. K., Japan

SO PCT Int. Appl., 100 pp.

CODEN: PIXXD2

DT Patent

LA Japanese

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.
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DATE

PI	WO 2000023610	A1	20000427	WO 1999-JP5817
	19991021			

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IE, SI, LT, LV, FI, RO
PRAI JP 1998-299962 A 19981021
WO 1999-JP5817 W 19991021

AB By inhibiting the signal transduction of TAK1, effects of inflammatory

cytokines are depressed, the production of inflammatory **cytokines** (IL-1, TNF, etc.) induced by inflammatory stimulus is depressed and the production of other inflammatory

cytokines (IL-6, etc.) induced by the inflammatory **cytokines** is depressed. The assay comprises contacting **TAK1** and **TAB1** (**TAK1** kinase binding protein 1) with the sample, monitoring formation of **TAK1** kinase-

TAK1 complexes, and screening compound that inhibits **TAK1-TAB1** binding. The method may also use labeled anti-TAB1 antibody for drug screening.

RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 11 OF 12 MEDLINE on STN DUPLICATE 4
AN 2000167218 MEDLINE
DN PubMed ID: 10702308
TI TAK1 mitogen-activated protein kinase kinase kinase is activated by
autophosphorylation within its activation loop.
AU Kishimoto K; Matsumoto K; Ninomiya-Tsuji J
CS Department of Molecular Biology, Graduate School of Science, Nagoya
University and CREST, Japan Science and Technology Corporation, Chikusa-ku, Nagoya 464-8602, Japan.
SO Journal of biological chemistry, (2000 Mar 10) 275 (10) 7359-64.
Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200004
ED Entered STN: 20000413
Last Updated on STN: 20000413
Entered Medline: 20000403
AB TAK1, a member of the mitogen-activated kinase kinase kinase family, is
activated in vivo by various **cytokines**, including interleukin-1 (IL-1), or when ectopically expressed together with the **TAK1**-binding protein **TAB1**. However, this molecular mechanism of activation is not yet understood. We show here
that endogenous **TAK1** is constitutively associated with **TAB1** and phosphorylated following IL-1 stimulation. Furthermore, TAK1 is constitutively phosphorylated when
ectopically overexpressed with TAB1. In both cases, dephosphorylation of
TAK1 renders it inactive, but it can be reactivated by preincubation with
ATP. A mutant of TAK1 that lacks kinase activity is not phosphorylated
either following IL-1 treatment or when coexpressed with **TAB1**, indicating that **TAK1** phosphorylation is due to autophosphorylation. Furthermore, mutation to alanine of a conserved
serine residue (Ser-192) in the activation loop between kinase domains VII
and VIII abolishes both phosphorylation and activation of TAK1. These

results suggest that **IL-1** and ectopic expression of **TAB1** both activate **TAK1** via autophosphorylation of Ser-192.

L5 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:256102 CAPLUS
DN 134:264947
TI Functional analysis of apoptosis signal-regulating kinase 1 (ASK
1)-binding proteins
AU Mochida, Yoshiyuki
CS Maxillofacial Surg., Maxillofacial Reconstruction Function., Div.
Maxillofacial Neck Reconstruction, Grad. Sch., Tokyo Med. Dent.
Univ.,
Japan
SO Kokubyo Gakkai Zasshi (2000), 67(2), 182-192
CODEN: KOGZA9; ISSN: 0300-9149
PB Kokubyo Gakkai
DT Journal
LA Japanese
AB Tumor necrosis factor (TNF) and interleukin-1 (**IL-1**)
are pleiotropic **cytokines** that activate two transcription
factors, Activator Protein-1 (AP-1) and Nuclear Factor- κ B
(NF- κ B). Apoptosis signal-regulating kinase 1 (ASK 1) is a
mitogen-activated protein (MAP) kinase kinase kinase (MAPKKK)
that is
activated by TNF and **IL-1**, and stimulates c-Jun
N-terminal kinase (JNK also known as SAPK; stress-activated
protein
kinase) and p38 activation. Through genetic screening for ASK
1-binding
proteins, Transforming Growth Factor β (TGF- β)-activated kinase
(TAK1), another MAPKKK family protein, was identified. Here we
report
that ASK 1 binds to TAK 1 and disassociates TAK 1 from TNF
receptor-associated
factor 6 (TRAF 6), and inhibits TAK 1- and TRAF 6-, but not
NF κ B-inducing kinase (NIK)-induced NF- κ B activation.

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